necessary. Extracts of the clones are aliquoted onto 0.25-inch filter disks, the solvent allowed to evaporate, and then placed on the surface of an overlay containing the assay organisms. Following incubation at appropriate temperatures, the diameter of the clearing zones is measured and recorded. Diode array HPLC, using authentic oxytetracyclin and tetracenomycin as standards, can be used to confirm expression of these antibiotics from the recombinant clones.

Please replace the original paragraph at page 55, lines 13-22 with the following paragraph:

Sequence analysis of chromosomally integrated pathways identified by screening can be performed for confirmation of the bioactive molecule. One approach which can be taken to rescue fosmid DNA from *S. lividans* clones exhibiting bioactivity against the test organisms is based on the observation that plasmid vectors containing IS*117*, such as pMF3, are present as circular intermediates at a frequency of 1 per 10-30 chromosomes. The presumptive positive clones can be grown in 25 ml broth cultures and plasmid DNA isolated by standard alkaline lysis procedures. Plasmid DNA preps are then used to transform *E. coli* and transformants are selected for Cm^r by plating onto LB containing chloramphenicol (15 mg/ml). Fosmid DNA from the *E. coli* Cm^r transformants is isolated and analyzed by restriction digestion analysis, PCR, and DNA sequencing.

IN THE CLAIMS:

Please enter the following rewritten claims:

16. (Amended) A method for identifying a DNA sequence which encodes a molecule or molecules which directly or indirectly modulate the interaction between at least a first and second molecule, comprising:

introducing into a cell containing interacting molecules which generate or repress a detectable signal or growth of the cell, genomic DNA or clones of a DNA library generated from nucleic acid derived from a mixed population of organisms and measuring the interaction of a first interacting molecule and a second interacting molecule in the presence of a third molecule encoded by the library or the genomic DNA or produced as a result of expression of one or more products encoded by the library or the genomic DNA, wherein interaction of the first and the second molecules in the absence of the third molecule produces a detectable signal or growth of the cell;

comparing the signal or growth of the cell in the presence and absence of the genomic DNA or library, wherein a difference between the response or growth is indicative of the presence of a molecule that modulates interaction between the first and second molecules; and

identifying a clone or DNA sequence which encodes a molecule or molecules which directly or indirectly modulates the interaction between the first and second molecules.

17. (Amended)The method of claim 16, wherein at least one of the interacting molecules contains a DNA-binding moiety and at least one of the interacting molecules contains a transcriptional activation or a transcriptional repressor moiety.

18. (Amended)The method of claim 17, wherein the DNA-binding moiety and the transcriptional activation moiety are derived from a single transcriptional activator.

19. (Amended)The method of claim 17, wherein the DNA-binding moiety and the transcriptional activation moiety are derived from different proteins.

20. (Amended) The method of claim 16, wherein the detectable signal is produced from a gene encoding a protein selected from the group consisting of β-galactosidase, green fluorescent protein, luciferase, alkaline phosphatase and chloramphenicol acetyl transferase.

22. (Amended)The method of claim 16, wherein the detectable signal is encoded by a gene present in a host cell.

23. (Amended)The method of claim 22, wherein the host cell further comprises a first recombinant gene encoding the first molecule, a second recombinant gene encoding the second molecule, or a third recombinant gene encoding the third molecule, wherein the first, second or third gene are expressed in the host cell.

24. (Amended) The method of claim 23, wherein the host cell contains both the first gene and the second gene.

25. (Amended) The method of claim 23, wherein the host cell contains the first, second and third genes.

26. (Amended) The method of claim 25, wherein the host cell is cultured under conditions that allows for expression of the genes.

27. (Amended) The method of claim 16, wherein the library is derived from an environmental sample.

28. (Amended) The method of claim 23, wherein the third gene is derived from an environmental library.

29. (Amended) The method of claim 16 or 28, wherein the environmental library is derived from an environmental sample comprising uncultured microorganisms.

30. (Amended) The method of claim 29, wherein uncultured microorganisms comprise a mixture of terrestrial microorganisms, a mixture of marine microorganisms, or a mixture of terrestrial and marine microorganisms.

31. (Amended) The method of claim 29, wherein the uncultured microorganisms are extremophiles.

32. (Amended) The method of claim 31, wherein the extremophiles are selected from the group consisting of thermophiles, hyperthermophiles, psychrophiles, and psychrotrophs.

33. (Amended) The method of claim 16 or 23, wherein the library is created by obtaining an environmental sample, enriching the environmental sample for eukaryotic organisms and selecting against prokaryotic organisms, isolating nucleic acids from the enriched sample, fractionating the nucleic acids, and cloning the isolated nucleic acids into a vector.

34. (Amended) The method of claim 33, wherein the nucleic acids are amplified prior to cloning into the vector.

35. (Amended) The method of claim 33, wherein the vector is an expression vector.

36. (Amended) A method for identifying a molecule that affects the interaction between a first and second molecule, comprising:

(i) contacting a first molecule with a second molecule in the presence of a third molecule derived from a library made from a mixed population of organisms or in the presence of the library or genomic DNA

wherein association of the first and second molecules in the absence of the third molecule results in the absence or presence of a detectable response by changing expression of a detectable gene or detectable gene product; and

(ii) comparing the detectable response in the presence of the third molecule with the detectable response in the absence of the third molecule, wherein a difference in response is indicative of the presence of a molecule that affects the interaction between a first and second molecule.

37. (Amended) The method of claim 36, wherein the detectable response is the expression or repression of a detectable gene.

38. (Amended) The method of claim 37, further comprising, prior to (i):

providing a prokaryotic host cell containing the detectable gene; and

providing a first gene expressed in the host cell, the first gene encoding the first molecule.

39. (Amended) The method of claim 38, further comprising, prior to (i):

providing a second gene expressed in the host cell, the second gene encoding the second molecule.

40. (Amended) The method of claim 39, further comprising, prior to (i):

providing a third gene expressed in the host cell, the third gene encoding the third molecule.

41. (Amended) The method of claim 40, further comprising, prior to (i):

introducing said first, second and third genes into the host cell; and

allowing expression of the genes.

42. (Amended) The method of claim 36, wherein the molecule contains a DNA binding domain and a transcriptional activation domain.

43. (Amended) The method of claim 36, wherein the interaction between the first and second molecules forms a transcriptional repressor.

44. (Amended) The method of claim36, wherein the third gene is derived from an environmental library.

45. (Amended) The method of claim36, further comprising, prior to (i):

obtaining an environmental sample; and

enriching the sample for prokaryotic organisms.

46. (Amended) The method of claim 45, further comprising producing a normalized library, comprising :

isolating nucleic acids from said enriched environmental sample;

fractionating the isolated nucleic acids;

melting the recovered fractions and allowing subsequent reannealing; and

amplifying any single-stranded nucleic acids present in the sample.